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FORM PTO 1590 (REV 5-93)		US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY DOCKET NUMBER 2002_0350A
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371			U.S. APPLICATION NO. (if known, see 37 CFR 1.51) NEW 10/070915
International Application No. PCT/NO00/00297	International Filing Date September 11, 2000	Priority Date Claimed September 13, 1999	
Title of Invention SINGLE STAGE SEED POLYMERISATION FOR THE PRODUCTION OF LARGE POLYMER PARTICLES WITH A NARROW SIZE DISTRIBUTION			
Applicant(s) For DO/EO/US Kari-Arne LETH-OLSEN, Øystein PAULSEN, Steinar PEDERSEN, Bård SAETHRE and Rolf Olaf LARSEN			
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:			
<ol style="list-style-type: none"><li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. §371.</li><li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. §371.</li><li>3. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1).</li><li>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</li><li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (in English) (35 U.S.C. §371(c)(2))<ol style="list-style-type: none"><li>a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</li><li>b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau.</li><li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US)</li></ol></li><li>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. §371(c)(2)).</li><li>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3)).<ol style="list-style-type: none"><li>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li><li>b. <input type="checkbox"/> have been transmitted by the International Bureau.</li><li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li><li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li></ol></li><li>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19.</li><li>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)). (unexecuted)</li><li>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)).</li></ol>			
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**10/070915**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :  
Kari-Anne LETH-OLSEN et al. : **Attn: BOX PCT**  
Serial No. NEW : **Docket No. 2002\_0350A**  
Filed March 13, 2002 :

SINGLE STAGE SEED POLYMERISATION  
FOR THE PRODUCTION OF LARGE  
POLYMER PARTICLES WITH A NARROW  
SIZE DISTRIBUTION  
[Corresponding to PCT/NO00/00297  
Filed September 11, 2000]

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents,  
Washington, DC 20231

Sir:

Please amend the above-identified application as follows:

**IN THE SPECIFICATION**

**Please rewrite the paragraph on page 4, lines 4-7 as follows:**

In order to describe prior art techniques in this field, reference will be made to the following patent specifications: NO 142082, NO 143403, NO 149108, NO 170730, NO 961625 (WO 97/40076), US 4,091,054, EP 0326383, EP 448391, US 4,382,124, EP 0 903 579 A1 and US 5,130,343.

**Please insert the following paragraphs on page 5, between lines 10 and 11:**

EP 0326383 discloses a seeded polymerisation wherein the start particles are dispersed in an organic solvent in which also the monomer is dissolved. The organic solvent is miscible with water. The process is characterised in that the solubility of the monomer in the solvent is reduced thereby

forcing the monomer into the start particles. Different means of reducing the solubility of the monomer in the solvent are described. It can be done by increasing the water concentration, by reducing the temperature, by adding water via a semipermeable membrane or by reducing the solvent concentration by evaporation.

Obvious disadvantages of this process are the use of large amounts of organic solvent and the need for measures to absorb the monomer into the start particles. The use of organic solvent will also to a large extent limit the versatility of this process to produce porous particles.

EP 448391 discloses a seed polymerisation using iterative steps to increase the particles size to the desired final particle size. Monomer is dosed in a strict controlled manner so the amount of free monomer in the system always is less than 10% of the amount of polymer present at any time during the polymerisation reaction. It is stated that if the amount of free monomer exceeds 10% there will be coagulation problems or there may be new formation of small particles which is highly undesirable. This gives a strong limitation of the process and it will never be possible to swell the polymer more than 1 time its own volume with new monomer. The total increase in diameter that is possible is 10 times. When, in addition, the start particles always are small (less than 2 microns are disclosed) a lot of iterative steps are necessary to achieve particles in the size range 10 to 50 microns.

#### IN THE CLAIMS

Cancel, without prejudice to the subject matter involved, claims 1-10.

Please add new claims 11-31 as follows:

11. (New) A procedure for producing spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range between 5 and 100  $\mu\text{m}$  by free radical polymerisation of vinyl monomers in water, characterised in that the polymerisation is performed as a one-step seed polymerisation wherein all of the monomer is added directly to the start particles which consist of a non-cross-linked polymer produced by a dispersion

polymerisation which gives the start particles such a high swelling capacity that they can absorb more than 5 times and preferably more than 20 times their own volume.

12. (New) A procedure in accordance with claim 11, characterised in that the start particles absorb from 5 to 120, preferably from 20 to 100, times their own volume of vinyl monomers or a mixture which contains vinyl monomers.

13. (New) A procedure in accordance with claim 12, characterised in that the mixture which contains vinyl monomers contains one or more inert solvents which lead to the formation of porosity in the polymer particles.

14. (New) A procedure in accordance with claim 13, characterised in that the mixture which contains vinyl monomers also contains a polymerisation initiator in addition to one or more inert solvents.

15. (New) A procedure in accordance with claim 14, characterised in that the polymerisation initiator is added separately from the mixture which contains vinyl monomers.

16. (New) A procedure in accordance with claim 11, characterised in that the vinyl monomers or a mixture which contains vinyl monomers is finely divided into small emulsion droplets before they are swelled into start particles.

17. (New) A procedure in accordance with claim 12, characterised in that the vinyl monomers or a mixture which contains vinyl monomers is finely divided into small emulsion droplets before they are swelled into start particles.

20. (New) A procedure in accordance with claim 15, characterised in that the vinyl monomers or a mixture which contains vinyl monomers is finely divided into small emulsion droplets before they are swelled into start particles.

22. (New) Spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range between 5 and 100  $\mu\text{m}$ , characterised in that they are produced by the procedure in accordance with claim 12.

24. (New) Spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range between 5 and 100  $\mu\text{m}$ , characterised in that they are produced by the procedure in accordance with claim 14.

25. (New) Spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range between 5 and 100  $\mu\text{m}$ , characterised in that they are produced by the procedure in accordance with claim 15.

26. (New) Polymer particles in accordance with claim 21, characterised in that the porous structure in the particles has a very low content of pores with a diameter below 50  $\text{\AA}$ , i.e. less than 10%, preferably less than 5%, of the total pore volume.

27. (New) Polymer particles in accordance with claim 21, characterised in that the porous structure in the particles is free from micropores with a diameter below 5  $\text{\AA}$ .

28. (New) Polymer particles in accordance with claim 26, characterised in that the porous structure in the particles is free from micropores with a diameter below 5  $\text{\AA}$ .

29. (New) Polymer particles in accordance with claim 21, characterised in that the size distribution of the polymer particles is always narrow and preferably narrower than that of the start particles.

30. (New) Polymer particles in accordance with claim 26, characterised in that the size distribution of the polymer particles is always narrow and preferably narrower than that of the start particles.

31. (New) Polymer particles in accordance with claim 27, characterised in that the size distribution of the polymer particles is always narrow and preferably narrower than that of the start particles.





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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**Please rewrite the paragraph on page 4, lines 4-7 as follows:**

In order to describe prior art techniques in this field, reference will be made to the following patent specifications: NO 142082, NO 143403, NO 149108, NO 170730, NO 961625 (WO 97/40076), US 4,091,054, EP 0326383, EP 448391, US 4,382,124, EP 0 903 579 A1 and US 5,130,343.

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Single stage seed polymerisation for the production of large polymer particles with a narrow size distribution

The present invention concerns large spherical polymer particles with a narrow size distribution and a procedure for producing such particles.

Polymer particles have today many areas of application such as separation, chromatography, adsorbents, ion exchangers, drug-delivery systems, solid-phase peptide synthesis, diagnostics and cosmetic preparations. Each application requires customised properties in the particles. The challenges involve controlling the particle size, the size distribution, the polymer composition, the porosity and the functionality.

Known techniques for the production of polymer particles are suspension polymerisation, emulsion polymerisation, miniemulsion polymerisation, microsuspension polymerisation and dispersion polymerisation. Suspension polymerisation is suitable for making large particles in the size range 0.05 to over 1 mm. The particle size is controlled by agitation and the type and concentration of suspending agents. The technique produces a very wide size distribution, which often limits the application possibilities. It is also difficult to achieve a desired size distribution when particles smaller than 100  $\mu\text{m}$  are to be produced. With miniemulsion and microsuspension polymerisation, prestabilised emulsion droplets of monomer are used to control the particle size. This also gives a very broad size distribution. With emulsion polymerisation, the particle size is controlled by the quantity and type of surfactants and not by mechanical agitation. This makes it possible to make very narrow size distributions, but the typical maximum particle size is approximately 1  $\mu\text{m}$ , and it is virtually impossible to make particles over approximately 10  $\mu\text{m}$  with this technique, which makes it unsuitable for making large polymer particles. Dispersion polymerisation differs from the above technologies in that the process is started in a homogeneous medium in which the monomer is soluble. When polymer is formed, it is precipitated as small particles that grow into the finished particles after the completion of the polymerisation. This process can produce narrow size distributions but in practice the maximum size is

limited to approximately 10 µm. Attempts to produce larger particles have mostly resulted in broad size distributions. Another limitation in this method is the problem of obtaining particles with a high degree of cross-linking. In this system, the introduction of cross-linking produces a wider size distribution and a high probability for the particles to coagulate.

Seed polymerisation is a further development of the methods mentioned above. This technique starts with already polymerised particles, start particles. In principle, start particles can be produced by any method. The start particles are dispersed in the reaction medium and new monomer and initiator are added so that the original particles grow into larger particles in a controlled process. As shown above, it is not, however, easy to produce large polymer particles in the size range 10 to 100 µm, or particles above 100 µm with a narrow size distribution. Seed polymerisation is the most appropriate technique for performing this task. However, the method is very limited because the ability of the polymer particles to absorb new monomer is low. The general rule is that new monomer can be absorbed in the ratio 1:1, maximum 5:1, relative to the volume of the start particles.

The absorption of monomer can be described using a thermodynamic swelling equation (Morton equation). The driving force for the diffusion of the monomer into the start particles is the partial molar energy of the mixture of monomer and polymer. However, the particles can only absorb a limited amount of monomer before the equilibrium swelling is achieved. The reason for this is that the swelling leads to an increase in the surface area of the particles and thus to increased surface free energy. This effect, which thus counteracts the swelling, is inversely proportional to the particle radius. The equilibrium swelling of the monomer can be calculated from the expression:

$$\Delta G_m = RT[\ln(\phi)_m + (1 - 1/J_p)\phi_p + \phi_p^2\chi + 2V_m\gamma/rRT] = 0$$

where  $\Delta G_m$  is the total partial molar free energy of the mixture,  $\phi_m$  and  $\phi_p$  are the volume fractions of the monomer and polymer respectively,  $J_p$  is the polymer's chain length,  $V_m$  is the monomer's partial molar volume,  $r$  and  $\gamma$  are the particles' radius and interfacial tension and  $\chi$  is Flory-Huggin's interaction constant.

5

The development of polymer particles that have permanent porosity, macroporous particles, is particularly interesting for their use as adsorbents, ion exchangers and chromatography media. It is known that such particles can be obtained by using an inert solvent together with the monomer mixture to be polymerised. It is also  
10 known that such solvents can be more or less good as solvents for the polymer formed. A soluble polymer can also be used as a pore forming agent. After the completion of polymerisation, the inert solvent and any soluble polymer are removed and a porous structure is obtained. In order to achieve a permanent porous structure, specific conditions must be present between the polymer formed  
15 and the solvent. The typical condition is that a cross-linked polymer is formed and that there is a complete phase separation between the polymer and the solvent. The size distribution of the pores formed is decisive for the area of application of the polymer particles. One known problem is that a considerable fraction of micropores less than 50 Å is formed. These are undesirable in separation  
20 processes because small molecules are left in the small pores and lead to poorer separation.

One main objective of the present invention is to produce compact and porous polymer particles and a procedure for producing such particles the above  
25 disadvantages. This and other objectives of the present invention are achieved as described in the claims.

The procedure is characterised in that a seed polymerisation is performed in which the start particles have a very high ability to absorb new monomer so that finished  
30 particles are obtained after only one polymerisation step even if the finished particles are to be as large as in the range 10 to 100 µm. The procedure is also characterised in that, when porous particles are produced, a porous structure can

be formed in which the fraction of micropores is insignificant. Another characteristic feature of the procedure is that the size distribution of the finished particles is narrow and in some cases narrower than in the start particles.

5 In order to describe prior art techniques in this field, reference will be made to the following patent specifications:  
NO 142082, NO 143403, NO 149108, NO 170730, NO 961625, US 4,091,054, US 4,382,124, EP 0 903 579 A1 and US 5,130,343.

10 NO 142082 and NO 143403 concern the technique that has become known as the two-step swelling method. The main element of this technique is that a low-molecular compound with very low water solubility is introduced into the start particles in a first stage. This results in an enormous increase in the particles' swelling capacity and much new monomer in relation to the polymer in the start particles can be absorbed and converted into polymer in a second step. The swelling ratio can be increased from 1:1-1:5 to 1:20-1:1000 times. NO 149108 also describes a two-stage swelling process. However, the special element of this method is that more swellable oligomer or oligomer-polymer particles are produced in the first stage. In these particles it is the oligomer content which

20 produces an increased swelling capacity instead of introducing a low-molecular compound with very low water solubility as in NO 142082 and NO 143403. In NO 170730, the disadvantages of these techniques are mentioned as being that they involve several stages to produce polymer particles over 10 µm since the start particles have a size of 0.5 µm.

25 NO 170730 concerns a process for producing particles in the size range 1 to 30 µm. In this process, start particles which are relatively large are used so that the swelling ratio can be small. Moreover, cross-linked start particles are used to avoid problems with coagulation, fusion and deformation of finished particles. A common feature with the first three references is that a first process stage is used involving the introduction of an activation agent (low-molecular compound with very low water solubility) to facilitate the absorption of new monomer in the second process stage. NO 961625 also uses relatively large start particles produced by dispersion

polymerisation. Here, the total swelling ratio is also large, but to obtain spherical particles can be obtained, the majority of the monomer must be introduced during polymerisation.

- 5 US 4,091,054 concerns a process which takes place without introducing an activation agent for swelling in a separate step. An initiator solution and a monomer solution are dosed continuously but separately to start particles with a defined size range in such a way that all the polymer is formed within the start particles. Since the monomer is polymerised continuously, the ratio between the  
10 monomer and the polymer is always low. This produces controlled but limited growth of the particles.

- US 4,382,124 concerns a traditional suspension polymerisation for the production of macroporous polymer particles. It describes how permanent porosity can be  
15 introduced into polymer particles. However, no measures are taken to control the size distribution or to prevent the formation of micropores.

- EP 0 903 579 A1 uses a technique very similar to that in NO 142082, NO 143403, NO 149108 and NO 170730 with regard to controlling the size and distribution of  
20 the particles but also describes new methods for avoiding micropores. This is achieved by introducing, together with the monomer, a compound with conjugated double bonds which does not react with the monomers, or the use of an oxidation-reduction reaction, or heat treatment of the finished particles.

- 25 US 5,130,343 also concerns a process similar to that in NO 142082, NO 143403, NO 149108 and NO 170730 with regard to controlling the particle size and distribution. A soluble polymer, which is used as the start particle, is extracted from the finished particle to form a macroporous structure.

- 30 In accordance with the present invention, unusual and unexpected results have surprisingly been found when a seed polymerisation is performed in which the start particles are produced by dispersion polymerisation. It is particularly advantageous to use a dispersion polymerisation as described in NO 970247, which patent

specification is hereby included as a reference in the present invention. Detailed descriptions of dispersion polymerisation are also provided in K. E. Barret, Br. Polym. J., 5,259, 1973 and E. Shen et al., J of Pol. Sci., 32, 1087, 1994.

5 The basis for the present invention is an aqueous dispersion of start particles. To this dispersion is then added the monomer mixture which is to be polymerised to form the finished particles. If porous particles are to be produced, the monomer mixture contains one or more pore forming agents. The polymerisation initiator may also be part of the monomer mixture or it may be added separately before or  
10 after the addition of the monomer. The volume ratio between the monomer mixture and start particles is always greater than 5:1. This means that the start particles constitute maximum 20% of the product particles and that the increase in particle diameter from start particle to product particle is always greater than 1.8. When the monomer mixture and the initiator are absorbed in the start particles, the  
15 polymerisation is performed conventionally at a temperature suitable to the initiator. The product particles are also processed conventionally by dewatering and washing to remove the stabilisers used to prevent flocculation and coagulation during polymerisation, unconverted monomers and initiator and pore forming agents if such agents have been used to make porous particles.

20

The new, special feature of this procedure is that a large amount of monomer can be absorbed in the start particles without using any form of low-molecular compound with low water solubility as a swelling aid and without the swelling taking place in many stages or by continuous dosing of monomer. The new  
25 procedure is thus very simple and is performed in its entirety in just one cycle by the monomer being swelled into the start particles directly in the desired quantity and the polymerisation being performed. The quantity of monomer which can be swelled in may be varied from 5 to more than 100 times the volume of the start particles. From a start particle of, for example, 5  $\mu\text{m}$ , it is possible to produce  
30 products with diameters from approximately 9 to approximately 25  $\mu\text{m}$  and from a start particle of, for example, 15  $\mu\text{m}$ , it is possible to produce products with

diameters between 25 and 75  $\mu\text{m}$ . There are no restrictions in the procedure with regard to the type of polymerisation additives which may be used.

- The types and quantities of emulsifiers, polymer stabilisers, initiators, inhibitors, monomers and solvents can be chosen freely depending on the polymer composition, porosity and particle size to be achieved. Different methods for dosing the monomer mixture may also be chosen. Different monomer mixtures will have different transport velocities through the aqueous phase in which they are added and into the start particles. For monomer systems with low water solubility, it may be advantageous to add the monomer as finely divided droplets, as this increases the transport velocity into the start particles, or partially water-soluble compounds may be added which also increase the transport velocity of the monomer.
- Typical monomers used in the monomer mixture are aromatic and aliphatic vinyl monomers such as styrene, vinyl toluene, vinyl pyridine, methyl acrylate, methyl methacrylate, butyl acrylate, butyl methacrylate, phenyl acrylate, phenyl methacrylate, glycidyl methacrylate, hydroxy ethyl methacrylate, methacrylic acid, acrylic acid, acrylamide and cross-linking agents such as divinyl benzene, ethylene glycol dimethacrylate, diallyl phthalate, divinyl pyridine and trivinyl benzene.
- Emulsifiers and suspension agents are used to keep the particles freely dispersed during the process and possibly also to wet and disperse the start particles. Examples of suitable substances are sodium lauryl sulphate, ammonium laurate, ammonium myristate, sodium dodecyl benzene sulphonate, alkyl sulphonate, sodium lauryl ether sulphate, sodium dihexyl sulphosuccinate, sodium dioctyl sulphosuccinate, fatty alcohol ethoxylate, sorbitan esters, polyvinyl alcohol, polymer cellulose ethers, polyvinyl pyrrolidone, magnesium silicate and calcium phosphate. Common polymerisation initiators such as the peroxides: benzoyl peroxide, lauryl peroxide, tert-butyl perbenzoate, didecanoyl peroxide, dioctanoyl peroxide and cumene hydroperoxide and the azo-initiators: azodiisobutyronitrile, azobismethylbutyronitrile and azobisdimethylvaleronitrile can be used.



Another surprising feature of the procedure is that the product particles have been shown to be completely spherical and free from defects; nor are there any problems with deformation and fusion of particles during the seed polymerisation even though the start particles are a non-cross-linked polymer.

5

Yet another surprising feature of the procedure is that the size distribution of the product particles is always narrow and in some cases narrower than the distribution of the start particles. This produces special advantages and degrees of freedom with regard to the use of start particles with a relatively broad size distribution even if a relatively narrow size distribution is required for the product. This means that start particles produced by dispersion polymerisation which are above 10  $\mu\text{m}$  and have a relatively broad distribution, as discussed above, are also well suited for the production of particles above 50  $\mu\text{m}$  which are to have a narrow size distribution.

15

The fact that the size distribution is narrower when a monomer mixture is swelled into start particles produced by dispersion polymerisation with a relatively high diameter and a relatively wide size distribution conflicts with the theory of equilibrium swelling, described above, if it is assumed that the molecular weight and surface conditions are equal for all start particles. The results indicate, therefore, that in a portion with start particles with a moderate size distribution, the smallest start particles will swell more than the largest start particles and the size will be equalised. This is very surprising.

20

Another surprising feature of the present invention is that the formation of micropores can be reduced considerably. This has not previously been possible without special measures, as described under the description of prior art techniques. One possible explanation is that the non-cross-linked polymer which constitutes the start particles contributes to a different phase separation in the system than when a cross-linked start particle is used.

25

30

The present invention will now be described in further detail using examples and figures that in no way restrict the possibilities of the present invention.

## DESCRIPTION OF FIGURES

Figure 1 shows a picture of the start particles from example A.1.

Figure 2 shows a picture of the start particles from example A.2.

5 Figure 3 shows a picture of the porous spherical polymer particles produced in accordance with example B.2.

Figure 4 shows a picture of the porous spherical polymer particles produced in accordance with example B.3.

Figure 5 shows a picture of the porous spherical polymer particles produced in  
10 accordance with example B.4.

The mean particle diameter and particle size distribution (CV) were determined using Coulter LS-230. CV is calculated by dividing the standard deviation (SD) by  
15 the mean particle diameter ( $d_p$ ):  $CV = (SD/d_p) * 100\%$ .

The specific surface area and pore volume were determined on the basis of  $N_2$  adsorption/desorption and a Hg porosimeter. A porosimeter (Units 120 and 2000) from Carlo Erba was used for the Hg measurements. The pore volume for pores  
20 with a diameter under 50 Å and pores with a diameter under 5 Å was determined on the basis of  $N_2$  adsorption/desorption using ASAP 2000 or Tristar 3000 from Micromeritics, USA.

## 25 EXAMPLES

### A. Production of start particles by dispersion polymerisation

Start particles were produced by dispersion polymerisation of methyl methacrylate  
30 in methanol with polyvinyl pyrrolidone (PVP K-30) as the stabiliser. Either 2,2-azobisisobutyronitrile (AIBN) or dioctanoyl peroxide was used as the initiator.

The following standard recipe was used:

Materials	Weight %
Methyl methacrylate	10 - 15
5 Methanol	80 - 85
PVP K-30	2.5 - 5
AIBN	0 - 0.4
Diocanoyl peroxide	0 - 0.4
Polymerisation temperature	50-58°C

10

Depending on the exact recipe, spherical particles were produced in the size range 1-15  $\mu\text{m}$  with a relatively narrow size distribution (CV 5-25%). When large start particles were produced, the size distribution was somewhat broader (CV 15-25%).

15

A constant polymerisation temperature was used throughout the polymerisation or the polymerisation temperature was controlled after the number of particles in the dispersion was constant (cf. patent NO 970247).

- 20 The following start particles were used for the production of large polymer particles with a narrow particle size distribution:

Example	Particle diameter ( $\mu\text{m}$ )	CV (%)
A.1	6	5
A.2	14	20
A.3	7	20

Figures 1 and 2 show pictures of the particles from examples A.1 and A.2

25 respectively.

B. One-step seed polymerisation for the production of large polymer particles with a narrow particle size distribution

Example B.1

5 A solution of methyl hydroxy propyl cellulose (0.7 g), sodium lauryl sulphate (0.5 g) and water (750 g) was mixed with a solution of styrene (38.0 g), ethylene glycol dimethacrylate (38.0 g), pentyl acetate (38 g) and azobismethylbutyronitrile (1.0 g). The mixture was emulsified using Ultra Turrax high-speed mixer and added to a reactor (5 l steel reactor). An aqueous dispersion of polymethyl methacrylate  
10 (PMMA) start particles produced in accordance with example A.1 (5.0 g start particles, 200 g water) and potassium iodide (0.2 g) were added to the reactor. The organic phase was left to swell into the start particles for 24 hours. Water (1500 g) was then added, after which the temperature was increased to 85°C. The polymerisation was completed in 7 hours at 85°C.

15

Porous spherical polymer particles with a mean diameter of 17  $\mu\text{m}$  and a CV of 16% were obtained. The specific surface area was 63  $\text{m}^2/\text{g}$  and the pore volume was 1.0  $\text{ml/g}$ . The pore volume for pores with a diameter below 50  $\text{\AA}$  was 0.015  $\text{ml/g}$  and for pores with a diameter less than 5  $\text{\AA}$  < 0.001  $\text{ml/g}$ .

20

Example B.2

A solution of methyl hydroxy propyl cellulose (0.7 g), sodium lauryl sulphate (0.5 g) and water (750 g) was mixed with a solution of methyl methacrylate (28 g), ethylene glycol dimethacrylate (84 g), pentyl acetate (48 g) and  
25 azobismethylbutyronitrile (1.0 g). The mixture was emulsified using Ultra Turrax high-speed mixer and added to a reactor (5 l steel reactor). An aqueous dispersion of PMMA start particles produced in accordance with example A.1 (5 g start particles, 174 g water) and potassium iodide (0.2 g) were added to the reactor. The organic phase was left to swell into the start particles for 2 hours. Water (1500  
30 g) was then added, after which the temperature was increased to 80°C. The polymerisation was completed in 7 hours at 80°C.

Porous spherical polymer particles with a mean diameter of 18  $\mu\text{m}$  and a CV of 20% were obtained; see Figure 3. The specific surface area was 50  $\text{m}^2/\text{g}$  and the pore volume was 0.4  $\text{ml/g}$ . The pore volume for pores with a diameter below 50  $\text{\AA}$  was 0.011  $\text{ml/g}$  and for pores with a diameter less than 5  $\text{\AA}$  0.004  $\text{ml/g}$ .

#### Example B.3

A solution of methyl hydroxy propyl cellulose (0.14 g), sodium lauryl sulphate (0.10 g) and water (110 g) was mixed with a solution of methyl methacrylate (7.60 g), ethylene glycol dimethacrylate (7.60 g), pentyl acetate (16.80 g) and azobismethylbutyronitrile (0.15 g). The mixture was emulsified using Ultra Turrax high-speed mixer and added to a reactor (0.5 l double-walled glass reactor). An aqueous dispersion of PMMA start particles produced in accordance with example A.2 (0.5 g start particles, 1.2 g water) was added to the reactor. The organic phase was left to swell into the start particles for 48 hours. Water (300 g) and potassium iodide (0.04 g) were then added, after which the temperature was increased to 80°C. The polymerisation was completed in 7 hours at 80°C.

Porous spherical polymer particles with a mean diameter of 55  $\mu\text{m}$  and a CV of 7% were obtained; see Figure 4. The specific surface area was 63  $\text{m}^2/\text{g}$  and the pore volume was 1.0  $\text{ml/g}$ . The pore volume for pores with a diameter below 50  $\text{\AA}$  was 0.011  $\text{ml/g}$  and for pores with a diameter less than 5  $\text{\AA}$  0.001  $\text{ml/g}$ .

#### Example B.4

A solution of methyl hydroxy propyl cellulose (0.14 g), sodium lauryl sulphate (0.10 g) and water (110 g) was mixed with a solution of styrene (7.60 g), ethylene glycol dimethacrylate (7.60 g), pentyl acetate (16.80 g) and azobismethylbutyronitrile (0.20 g). The mixture was emulsified using Ultra Turrax high-speed mixer and added to a reactor (0.5 l double-walled glass reactor). An aqueous dispersion of PMMA start particles produced in accordance with example A.2 (0.5 g start particles, 41.2 g water) was added to the reactor. The organic phase was left to swell into the start particles for 48 hours. Water (300 g) and potassium iodide (0.04 g) were then added, after which the temperature was increased to 80°C. The polymerisation was completed in 7 hours at 80°C.

Porous spherical polymer particles with a mean diameter of 50  $\mu\text{m}$  and a CV of 9% were obtained; see Figure 5. The specific surface area was 68  $\text{m}^2/\text{g}$  and the pore volume was 1.0  $\text{ml/g}$ . The pore volume for pores with a diameter below 50  $\text{\AA}$  was 0.017  $\text{ml/g}$  and for pores with a diameter less than 5  $\text{\AA}$  < 0.0001  $\text{ml/g}$ .

5

#### • Example B.5

• A solution of methyl hydroxy propyl cellulose (0.14 g), sodium lauryl sulphate (0.10 g) and water (110 g) was mixed with a solution of methyl methacrylate (4.8 g), ethylene glycol dimethacrylate (14.4 g), pentyl acetate (12.8 g) and  
10 azobismethylbutyronitrile (0.20 g). The mixture was emulsified using Ultra Turrax high-speed mixer and added to a reactor (0.5 l double-walled glass reactor). An aqueous dispersion of PMMA start particles produced in accordance with example A.3 (1.0 g start particles, 41.6 g water) and potassium iodide (0.04 g) were added to the reactor. The organic phase was left to swell into the start particles for 2  
15 hours. Water (300 g) was then added, after which the temperature was increased to 60°C. The polymerisation was completed in 7 hours at 60°C.

Porous spherical polymer particles with a mean diameter of 24  $\mu\text{m}$  and a CV of 18% were obtained. The specific surface area was 129  $\text{m}^2/\text{g}$  and the pore volume  
20 was 0.7  $\text{ml/g}$ . The pore volume for pores with a diameter below 50  $\text{\AA}$  was 0.045  $\text{ml/g}$  and for pores with a diameter less than 5  $\text{\AA}$  < 0.0001  $\text{ml/g}$ .

## CLAIMS

1. A procedure for producing spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range  
5 between 5 and 100  $\mu\text{m}$  by free radical polymerisation of vinyl monomers, characterised in that the polymerisation is performed as a one-step seed polymerisation in which the start particles consist of a non-cross-linked polymer produced by a dispersion polymerisation which gives the start particles  
10 such a high swelling capacity that they can absorb more than 5 times and preferably more than 20 times their own volume.
2. A procedure in accordance with claim 1, characterised in that  
15 the start particles absorb from 5 to 120, preferably from 20 to 100, times their own volume of vinyl monomers or a mixture which contains vinyl monomers.
3. A procedure in accordance with claim 2, characterised in that  
the mixture which contains vinyl monomers contains one or more inert solvents which lead to the formation of porosity in the polymer particles.
- 20 4. A procedure in accordance with claim 3, characterised in that the mixture which contains vinyl monomers also contains a polymerisation initiator in addition to one or more inert solvents.
5. A procedure in accordance with claim 4, characterised in that  
25 the polymerisation initiator is added separately from the mixture which contains vinyl monomers.
6. A procedure in accordance with claims 1 to 5, characterised in  
30 that the vinyl monomers or a mixture which contains vinyl monomers is finely divided into small emulsion droplets before they are swelled into the start particles.

7. Spherical polymer particles with a narrow size distribution, i.e. with a CV of less than 35%, preferably less than 20%, in the range between 5 and 100  $\mu\text{m}$ , characterised in that they are produced by the procedure in accordance with claims 1-6.

5

8. Polymer particles in accordance with claim 7, characterised in that the porous structure in the particles has a very low content of pores with a diameter below 50  $\text{\AA}$ , i.e. less than 10%, preferably less than 5%, of the total pore volume.

10

9. Polymer particles in accordance with claim 7 or 8, characterised in that the porous structure in the particles is free from micropores with a diameter below 5  $\text{\AA}$ .

15 10. Polymer particles in accordance with claim 7, 8 or 9, characterised in that the size distribution of the polymer particles is always narrow and preferably narrower than that of the start particles.



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(54) Title: SINGLE STAGE SEED POLYMERISATION FOR THE PRODUCTION OF LARGE POLYMER PARTICLES WITH A NARROW SIZE DISTRIBUTION

(57) Abstract: The present invention concerns large spherical polymer particles with a narrow size distribution and a procedure for producing such particles. The procedure is characterised in that a seed polymerisation is performed in which the start particles have a very high ability to absorb new monomer so that finished particles are obtained after only one stage of polymerisation even if the finished particles are to be as large as in the range 10 to 100 µm. The procedure is also characterised in that, when porous particles are produced, a porous structure can be formed in which the fraction of micropores is insignificant. Another characteristic feature of the procedure is that the size distribution of the finished particles is narrow and in some cases narrower than in the start particles.

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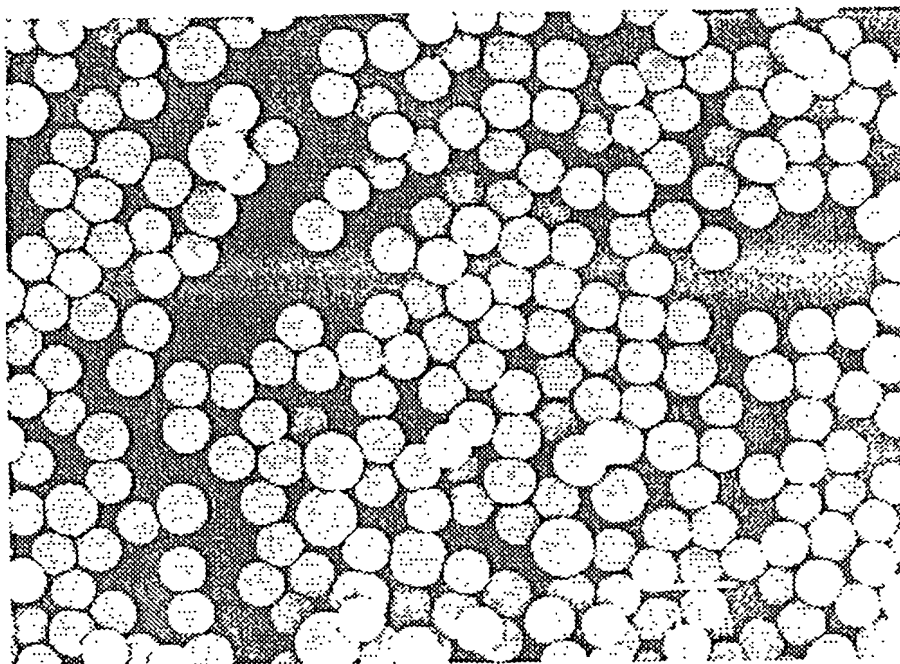


Fig. 1: SEM picture of start particles produced in accordance with example A.1

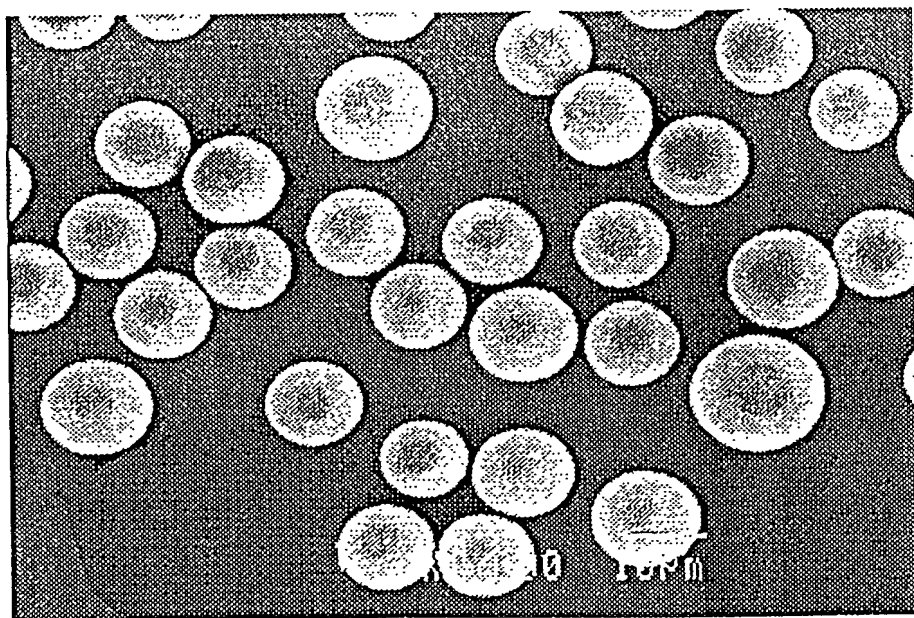


Fig.2: SEM picture of start particles produced in accordance with example A.2

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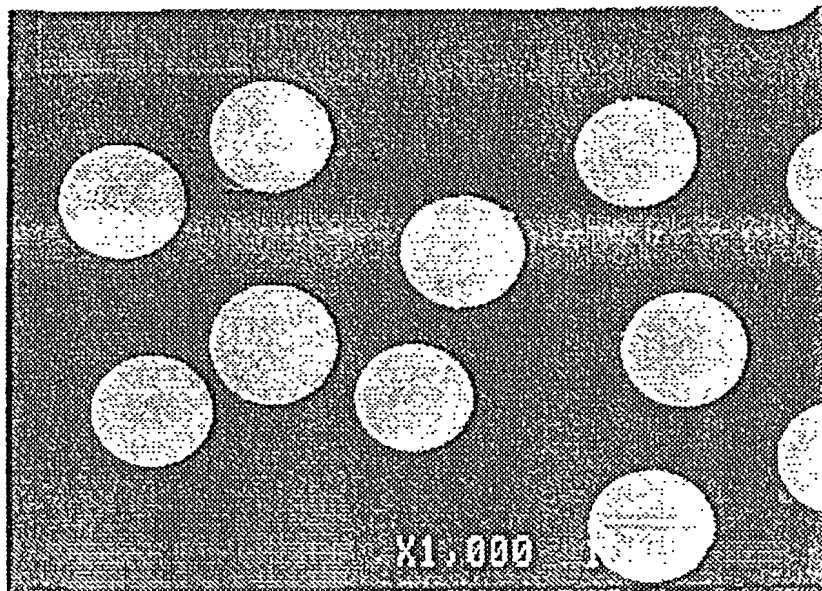


Fig. 3: SEM picture of polymer particles produced in accordance with example B.2

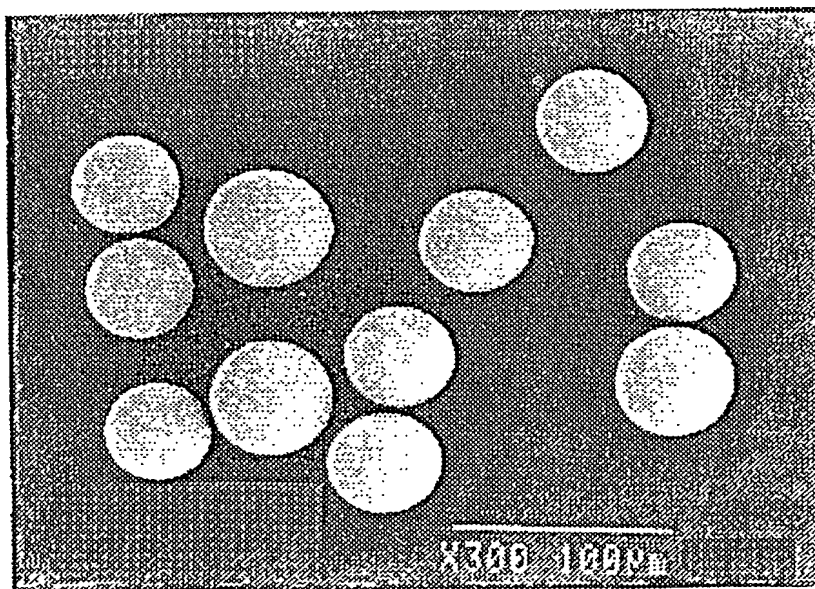


Fig. 4: SEM picture of porous particles produced in accordance with example B.3

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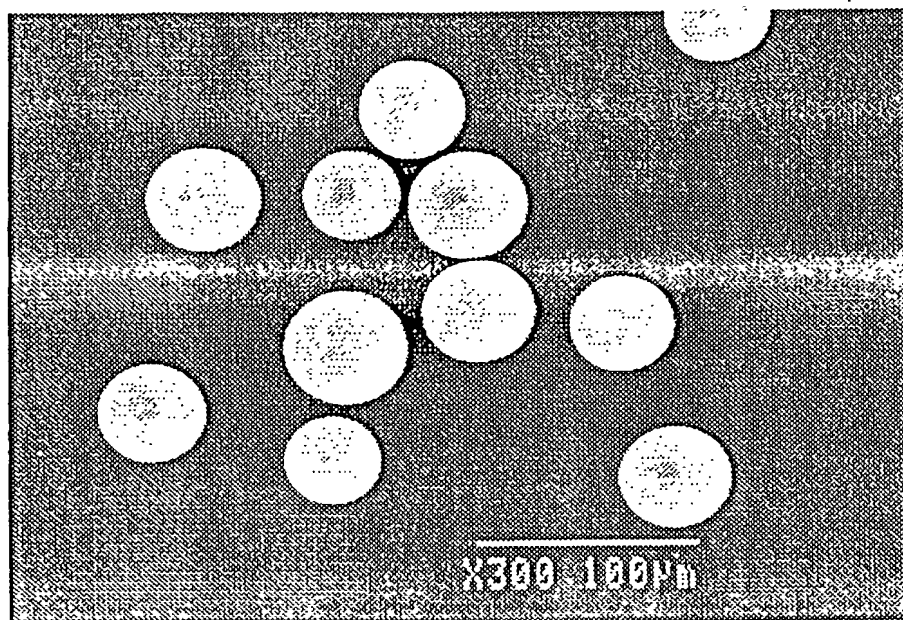


Fig. 5: SEM picture of porous particles produced in accordance with example B.4

## DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATION

( ) Original ( ) Supplemental ( ) Substitute (X) PCT ( ) Design

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**"Single stage seed polymerisation for the production of large polymer**

Title: particles with a narrow size distribution"

of which is described and claimed in:

- ( ) the attached specification, or  
 ( ) the specification in the application Serial No. \_\_\_\_\_ filed \_\_\_\_\_;  
 and with amendments through \_\_\_\_\_ (if applicable), or  
 (X ) the specification in International Application No. PCT/ NO00/00297, filed 11.09.2000, and as amended  
 on 10.09.2001 (if applicable).

I hereby state that I have reviewed and understand the content of the above-identified specification, including the claims, as amended by any amendment(s) referred to above.

I acknowledge my duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, ' 1.56.

I hereby claim priority benefits under Title 35, United States Code, ' 119 (and ' 172 if this application is for a Design) of any application(s) for patent or inventor's certificate listed below and have also identified below any application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:


COUNTRY	APPLICATION NO.	DATE OF FILING	PRIORITY CLAIMED
NO	19994425	13.09.1999	YES

I hereby claim the benefit under Title 35, United States Code ' 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code ' 112, I acknowledge the duty to disclose information material to patentability as defined in Title 37, Code of Federal Regulations, ' 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

APPLICATION SERIAL NO.	U.S. FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

And I hereby appoint Michael R. Davis, Reg. No. 25,134, Matthew M. Jacob, Reg. No. 25,154; Warren M. Cheek, Jr., Reg. No. 33,367; Nils Pedersen, Reg. No. 33,145; Charles R. Watts, Reg. No. 33,142; and Michael S. Huppert, Reg. No. 40,268, who together constitute the firm of WENDEROTH, LIND & PONACK, L.L.P., as well as any other attorneys and agents associated with Customer No. 000513, to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith.

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I further declare that all statements made herein of my own knowledge are true, and that all statements on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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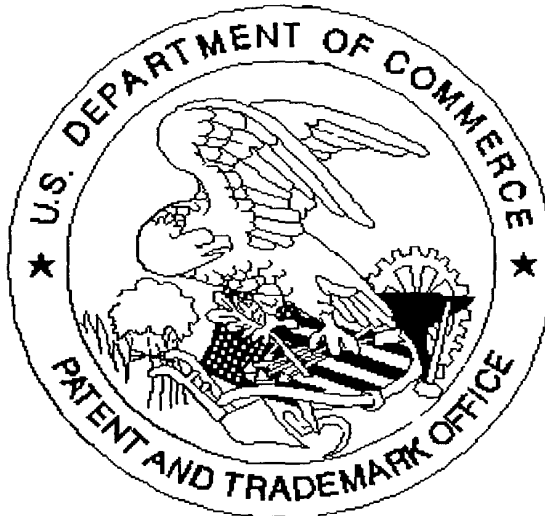
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Title of Invention SINGLE STAGE SEED POLYMERISATION FOR THE PRODUCTION OF LARGE POLYMER PARTICLES WITH A NARROW SIZE DISTRIBUTION

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